

**REMARKS**

Claims 1-18, 20-29, 31-32, and 37-42, all the claims pending in the application, stand rejected on prior art grounds. Claims 19, 30, and 33-36 have been previously canceled without prejudice or disclaimer. Claims 1, 6, 10, 24-28, and 37 are amended herein. Applicants respectfully traverse the rejections based on the following discussion.

**I. The Prior Art Rejections**

Claims 1-13, 16-18, 20, 24-28, and 37-42 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Mirkin (U.S. Patent Publication No. 2004/0131843), hereinafter referred to as "Mirkin (843)" and Mirkin (U.S. Publication No. 2002/0063212), hereinafter referred to as "Mirkin (212)", in view of Cubicciotti (U.S. Patent No. 6,762,025). Claims 14, 15, 21-23, 28, and 29 stand rejected under 35 USC 103(a) as being unpatentable over Mirkin (843), Mirkin (212), Cubicciotti, in view of Colbert (U.S. Publication No. 2003/0106998).

Generally, the Office Action states that Cubicciotti discloses that separation of the surfaces is achieved by template-directed attachment of an effector molecule; e.g., a nanosphere to a first surface, and refers to column 39, lines 41-52 of Cubicciotti for this teaching (page 4 of Office Action). The Office Action also states that Cubicciotti discloses that "proximity-based methods for single-molecule detection include proximal probe methods (e.g. – AFM, STM) with reporter molecules (e.g., macromolecules, polymers, or preferably nanopartilces or microparticles) to select and isolate...." (page 4 of Office Action). The Office Action also states that "[s]ingle-molecule affinity selection can be achieved by immobilizing a target molecule to an SPM tip (i.e., negatively charged silicon nitride) used to probe a random-sequence,

nanosphere-conjugated nucleic acid library.” (page 4 of Office Action).

The Office Action goes on to state that portions of Cubicciotti, combined with Mirkin (843) and Mirkin (212) render the Applicants’ invention obvious. The Applicants respectfully disagree. While Cubicciotti describes the use of nanoparticles, it does not anywhere describe affixing them to a tip, which the Applicants’ claimed invention clearly provides. Cubicciotti’s use of nanoparticles is to place them on a surface and allow them to selectively bind to target molecules. After binding, SPM imaging is used to see where the nanoparticles are fixed. Note here that Cubicciotti places nanoparticles on a surface, rather than on a SPM tip (see column 39, lines 41-52).

Cubicciotti’s second described method is for fixing the target molecule to an SPM tip and then scanning it over a surface covered with a “nanosphere-conjugated nucleic acid library.” (column 157, line 67). Again here, the nanospheres (or nanoparticles) are on the surface to be scanned, rather than on the SPM tip. In this case it is a target molecule (and not a nanoparticle) that is fixed to the SPM tip.

In summary, although Cubicciotti describes nanoparticles, and also discusses the use of SPM tips for single-molecule detection, he nowhere mentions the use of these nanoparticles in the manner that the Applicants’ claimed invention does – that is, affixing one or more of the nanoparticles to the SPM tip.

The Office Action also suggests that the Applicants’ claims are anticipated by Mirkin (843) and Mirkin (212). According to the Office Action, Mirkin 843 generally discloses the following three features:

- (1) “An apparatus and method for dip pen lithography where a probe tip is coated

with a patterning compound that includes a nanoparticle-containing additive. The coating is applied by dipping the probe tip in a solution of the patterning compound.” (page 2 of Office Action)

The Applicants respectfully but strongly disagree that Mirkin 843 discloses what the Office Actions says it does. Examiner cites paragraphs [0015], [0053], and [0093] as evidence for the above disclosure. However, in none of these paragraphs, or for that matter in any other paragraph, does Mirkin 843 discuss any “nanoparticle containing additives.” Mirkin 843 discusses many different possible patterning compounds in paragraphs [0055] - [0074], however they are all different types of molecules, and not nanoparticles, as in the Applicants’ claimed invention.

Furthermore, the Applicants strongly disagree that Mirkin 843 discloses a method for coating a probe tip with a patterning compound. Paragraph [0015] of Mirkin 843 specifically states describes: “The method comprising...coating the tip with a solution of the patterning compound, and contacting the coated tip with the substrate so that the compound is applied to the substrate so as to produce a desired pattern.” From this sentence it is clear that the patterning compound is never applied to the tip, rather it remains in solution when coating the tip. In fact, it is contrary to Mirkin 843’s invention to have the compound coating the tip, since the goal (as stated in paragraph [0015]) is to transfer the patterning compound to the substrate. This is directly counter to the Applicants’ claimed invention, in which nanoparticles are attached permanently to the tip.

(2) “A variety of patterning compounds that include nanoparticles.”

Applicants strongly disagree that Mirkin 843 discloses patterning compounds that include

nanoparticles. The Office Action cites paragraphs [0056]-[0072], [0081], and [0089] in support of this statement. As noted above, [0055] - [0074] provide a long list of possible patterning compounds, all of which are molecular compounds. However, none of these describe nanoparticles. Paragraph [0081] describes a method by which force can be applied between tip and sample – in this case, a method for applying a magnetic force. Mirkin 843 states that this can be done: “with a magnetic material located behind the tip by a current-carrying coil.” However, there is no mention of nanoparticles in relation to this method, or in fact of anything attached to a tip. Paragraph [0089] describes patterning of arrays by Mirkin’s technique. Specifically, this paragraph describes arrays of biological materials. However, there is no mention of nanoparticles in this paragraph or in any other paragraph. Furthermore, this paragraph does not describe attaching anything to a tip, let alone attaching a nanoparticle to a tip.

(3) “The use of 13 and 20nm nanoparticles.”

Mirkin 843 may describe the use of 13 and 20nm nanoparticles. However, Applicants strongly disagree that Mirkin’s use could be augmented in the manner to stick nanoparticles on a tip. The Office Action cites paragraphs [0109] and [0114] in support of the argument. Paragraph [0109] describes: “a structure-forming compound comprising oligonucleotide strand B attached to 13nm nanoparticles was applied as described above.” Paragraph [0105] describes this method: “Structure-forming compound B was applied to the substrate by immersing the substrate in a solution of the compound for an hour at room temperature so that the oligonucleotide strand B hybridized to oligonucleotide C.” It is noteworthy that this discussion involves attaching the 13nm nanoparticles (with oligonucleotide strand B attached) to the substrate, and not to a tip. Indeed, the essence of Mirkin 843’s invention is that structures are attached to substrates, and not

the tips used to pattern the substrates. Paragraph [0114] is a different example involving 20nm gold nanoparticles, however again these nanoparticles are affixed to oligonucleotide strand D and then attached to a substrate, and not a tip. [0114] notes: "oligonucleotide strand D attached to 20nm gold nanoparticles was prepared and applied to the substrate as described in Example 1...."

Again, nanoparticles have not been used in SPM before because there did not exist a good method for attaching nanoparticles to SPM tips. The claimed invention further includes an adhesion promoter (adhesion layer) to better affix the nanoparticles to the probe tip. Clearly, there is no teaching in Anstadt of using an adhesion promoter to facilitate the adherence of the nanoparticles to the respective surface. Additionally, the adhesive layer described in paragraph [0055] of Colbert relates to nanotube assemblies, which as further explained below, is a separate and wholly unique application the claimed invention's nanoparticle assemblies.

Insofar as references may be combined to teach a particular invention, and the proposed combination of Mirkin (843), Mirkin (212), Cubicciotti, and Colbert in various combinations with one another, case law establishes that, before any prior-art references may be validly combined for use in a prior-art 35 U.S.C. § 103(a) rejection, the individual references themselves or corresponding prior art must suggest that they be combined.

For example, in In re Sernaker, 217 U.S.P.Q. 1, 6 (C.A.F.C. 1983), the court stated: "[P]rior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantage to be derived from combining their teachings." Furthermore, the court in Uniroyal, Inc. v. Rudkin-Wiley Corp., 5 U.S.P.Q.2d 1434 (C.A.F.C. 1988), stated, "[w]here prior-art references require selective combination by the court to render

obvious a subsequent invention, there must be some reason for the combination other than the hindsight gleaned from the invention itself . . . Something in the prior art must suggest the desirability and thus the obviousness of making the combination."

In the present application, the reason given to support the proposed combination is improper, and is not sufficient to selectively and gratuitously substitute parts of one reference for a part of another reference in order to try to meet, but failing nonetheless, the Applicants' novel claimed invention. Furthermore, the claimed invention, as amended, meets the above-cited tests for obviousness by including embodiments such as having generally spherical nanoparticles affixed to the microscope tip and coating the microscope tip with an adhesion promoter prior to affixing the nanoparticles thereon. As such, all of the claims of this application are, therefore, clearly in condition for allowance, and it is respectfully requested that the Examiner pass these claims to allowance and issue.

As declared by the Federal Circuit:

In proceedings before the U.S. Patent and Trademark Office, the Examiner bears the burden of establishing a prima facie case of obviousness based upon the prior art. The Examiner can satisfy this burden only by showing some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references. In re Fritch, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992) citing In re Fine, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

Here, the Examiner has not met the burden of establishing a prima facie case of obviousness. It is clear that, not only does each of Mirkin (843), Mirkin (212), Cubicciotti, and Colbert individually fail to disclose all of the elements of the claims of the claimed invention, particularly, a scanning probe microscope tip having an adhesion promoter thereon and coated with a layer of chemically-synthesized generally spherical nanoparticles affixed to the tip, as

discussed above, but also, a combination of Mirkin (843), Mirkin (212), Cubicciotti, and Colbert fails to disclose these elements as well. The unique elements of the claimed invention are clearly an advance over the prior art.

The Federal Circuit also went on to state:

The mere fact that the prior art may be modified in the manner suggested by the Examiner does not make the modification obvious unless the prior art suggested the desirability of the modification. . . . Here the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered obvious. This court has previously stated that one cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention. Fritch at 1784-85, citing In re Gordon, 221 U.S.P.Q. 1125, 1127 (Fed. Cir. 1984).

Here, there is no suggestion that Mirkin (843), Mirkin (212), Cubicciotti, and Colbert alone or in combination with one another, teaches a structure and method containing all of the limitations of the claimed invention. Consequently, there is absent the "suggestion" or "objective teaching" that would have to be made before there could be established the legally requisite "prima facie case of obviousness."

Additionally, clearly the invention is part of a crowded art field. As such, given the crowdedness of the art, the novel aspects of the invention should be regarded as a significant step forward in the constant development of this technical art field. Moreover, given that at least three separate references, and in some cases four separate references must be combined with one another is evidence of unobviousness.

Again, Mirkin (843) merely discloses a method of nanolithography utilizing a scanning probe microscope tip to pattern a substrate passivated with a resist using a patterning compound. Contrary to the assertion in the Office Action, the patterning compound is a molecular compound

transferred to a substrate, not a nanoparticle affixed to a scanning probe microscope tip.

Accordingly, Mirkin (843) is structurally and functionally distinct and not equivalent to the claimed invention. (See Mirkin at Abstract; and Paragraphs [0001] and [0006]).

Applicants respectfully submit that the Office Action misinterprets Mirkin (843) in the Office Action. Although the Office Action cites paragraphs [0015], [0053], and [0093] as evidence of Applicants' claimed invention, none of these paragraphs, or for that matter any other paragraph in Mirkin (843), appear to discuss any "nanoparticle containing additives." Instead, Mirkin (843) discusses many different possible patterning compounds, however these patterning compounds are all different types of molecules; not nanoparticles as claimed by Applicant. (See Office Action, Page 2-3, Section 3; and Mirkin (843). Paragraphs [0055]-[0074]).

Accordingly, Mirkin (843) does not teach nanoparticles being affixed to a tip, let alone, an outer coating layer of a nanoparticle. Therefore, Mirkin (843) does not disclose, teach or suggest, including each of the nanoparticles includes an outer coating layer encapsulating each nanoparticle. Mirkin (212) is also deficient.

In contrast, Figures 27A and 27B of Mirkin (212) merely disclose "dip pen" lithography using a scanning probe microscope where a tip is coated with a patterning compound comprised of molecular compounds and delivered from the tip to a substrate. Although Mirkin (212) is primarily focused on using molecular compounds as a patterning compound, Mirkin (212) does suggest a single particle array formed on 300nm or 700 nm dots. However, Mirkin (212) like Mirkin (843) discloses that the patterning compound is easily removable from the tip surface with a suitable solvent, and thus is not affixed to the tip like Applicants' invention. (See Office Action, Page 3, Paragraph 3; Mirkin (212) at Abstract; Page 4, Paragraphs [0049] and [0054];



Page 24, Paragraph [0209]; and Figures 27A and 27B).

Indeed, Mirkin (212) appears to suggest coating a tip of the scanning probe microcroscope, not a coating over each single particle of the array. Therefore, Mirkin (212) does not disclose, teach or suggest, including each of the nanoparticles includes an outer coating layer encapsulating each nanoparticle as claimed by Applicants.

In comparison, Applicants' claimed invention includes a scanning probe microscope tip 1 where nanoparticles 2 are affixed to the scanning probe microscope tip 1, and each nanoparticle is encapsulated by an outer coating layer 3. The nanoparticles 2, for example, as recited in claim 31, may include cobalt nanoparticles. Further, the outer coating layer 3, for example, as recited in claim 32, may include a single molecular layer of oleic acid. (See Application, Page 7, line 20-Page 8, line 1).

As discussed above, Mirkin (843) only discloses molecular compounds and Mirkin (212) primarily discloses molecular compounds and suggests single particles as patterning compounds, though neither reference discloses or suggests any outer coating layer encapsulating the molecular compounds or the single particles. Accordingly, the claimed invention provides a structure, which improves the spatial resolution of a scanning probe microscope when compared with either of the conventional Mirkin inventions.

Thus, Applicants traverse the assertion that Mirkin (843) and Mirkin (212) teach Applicants' claimed invention. For at least the reasons outlined above, Applicants respectfully submit that neither Mirkin (843) nor Mirkin (212), alone or in combination, disclose, teach or suggest, including each of the nanoparticles includes an outer coating layer encapsulating each nanoparticle.

Indeed, the Applicants agree with the Office Action that neither Mirkin (843), Mirkin (212), or Cubicciotti disclose the use of adhesion layers and annealing, as well as the above claimed feature, and thus these references are deficient in that they do not disclose Applicants' claimed invention. (See previous Office Action, Page 4, lines 1-9). Colbert is also deficient.

In contrast, Colbert merely discloses macroscopically manipulable nanoscale devices made from nanotube assemblies. As described in highly specific detail in the previous Amendment, Applicants clearly describe that Colbert is focused on using molecular nanotubes to fabricate devices that enable interaction between macroscopic systems and individual objects having nanometer dimension without disclosing or suggesting the use of nanoparticles like Applicants' claimed invention.

For emphasis, as indicated in Colbert, "in a preferred form this device comprises a nanotube probe tip assembly made up of one or more single-wall and/or multi-wall nanotubes." Accordingly, Colbert teaches away from using the smaller nanoparticles. Indeed, Applicants agree with the Office Action that Colbert as well as Mirkin (843) and Mirkin (212) and Cubicciotti fail to teach the use of spherical nanoparticles attached to a tip. Clearly, Colbert does not disclose or teach the use of any nanoparticles, let alone, spherical nanoparticles or a coating encapsulating nanoparticles. Therefore, Colbert does not teach or suggest including each of the nanoparticles includes an outer coating layer encapsulating each nanoparticle.

Applicants' claimed invention, as discussed above, includes nanoparticles 2 encapsulated with an outer coating layer 3, whereas Colbert only discloses nanotubes, not nanoparticles, let alone, nanoparticles encapsulated with an outer coating layer. Thus, Applicants traverse the assertion that Colbert teaches Applicants' invention.

For at least the reasons outlined above, Applicants respectfully submit that none of Mirkin (843), Mirkin (212), Cubicciotti, nor Colbert, alone or in combination, disclose, teach or suggest, including each of the nanoparticles includes an outer coating layer encapsulating each nanoparticle.

In view of the foregoing, the Applicants respectfully submit that the collective cited prior art do not teach or suggest the features defined by independent claims 1, 10, 24-28, 37, 38, and 42, and as such, claims 11, 10, 24-28, 37, 38, and 42 are patentable over Mirkin (843), Mirkin (212), Cubicciotti, and Colbert alone or in combination with one another. Further, dependent claims 2-9, 11-18, 20-23, 29, 31-32, and 39-41 are similarly patentable over Mirkin (843), Mirkin (212), Cubicciotti, and Colbert alone or in combination with one another, not only by virtue of their dependency from patentable independent claims, respectively, but also by virtue of the additional features of the invention they define. Thus, the Applicants respectfully request that these rejections be reconsidered and withdrawn.

Moreover, the Applicants note that all claims are properly supported in the specification and accompanying drawings, and no new matter is being added. In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections.

## **II. Formal Matters and Conclusion**

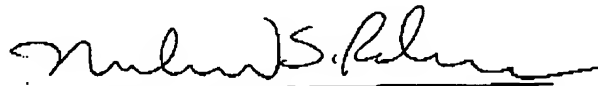
In view of the foregoing, the Applicants submit that claims 1-18, 20-29, 31-32, and 37-42, all the claims presently pending in the application, are patentably distinct from the prior art of record and are in condition for allowance. Furthermore, no new matter is presented. The Examiner is respectfully requested to pass the above application to issue at the earliest possible

time.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at the local telephone number listed below to discuss any other changes deemed necessary. Please charge any deficiencies and credit any overpayments to Attorney's Deposit Account Number 50-0510.

Respectfully submitted,

Dated: October 7, 2005



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